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N
    85650-52-8 REGISTRY
    Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,24b-hexahydro-2-
CN
    methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-
    methyl-, (.+-.)-
OTHER NAMES:
ĆN----
    -6-Azamianserin)
CN
    Mepirzapin
CN
    Mepirzepine
CN-
    Mirtazapine
CN
    Mirtazepine
CN
    Mirtazipine
CN
    Org 3770
CN
    Promyrtil
CN
    Remergil
CN
     Remergon
CN
    Remeron
CN
     Rexer
CN
     Zispin
FS
     3D CONCORD
    61337-67-5, 82601-27-2
DR
MF
    C17 H19 N3
CI
    COM
    Commission of European Communities
SR
                ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS,
ĹC
    STN Files:
      BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU,
    DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       MSDS-OHS, PHAR, PIRA, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2,
      USPATFULL
         (*File contains numerically searchable property data)
    Other Sources: EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

289 REFERENCES IN FILE CA (1957 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
289 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> file medicine

ACCESSION NUMBER:

58818 EMBASE 1996158818

DOCUMENT NUMBER: TITLE:

Mirtazapine. A review of its pharmacology and therapeutic

potential in the management of major depression.

AUTHOR:

Davis R.; Wilde M.I.

CORPORATE SOURCE:

Adis International Limited, 41 Centorian Drive, Mairangi

Bay, Auckland 10, New Zealand CNS Drugs, (1996) 5/5 (389-402).

ISSN: 1172-7047 CODEN: CNDREF

COUNTRY:

SOURCE:

New Zealand

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT:

Psychiatry 032

037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE:

English

SUMMARY LANGUAGE: English

Mirtazapine is a tetracyclic antidepressant with a novel mechanism of action; it increases noradrenergic and serotonergic neurotransmission via blockade of central .alpha.2-adrenergic auto-and heteroreceptors. The increased release of serotonin (5-hydroxytryptamine; 5-HT) stimulates serotonin 5-HT1 receptors because mirtazapine directly blocks 5-HT2 and 5-HT3 receptors. The enhancement of both noradrenergicand 5-HT1 receptor-mediated neurotransmission is thought to be responsible for the antidepressant activity of mirtazapine. In short term (5 to 6 weeks) clinical trials in patients with depression, mirtazapine produces clinical improvements significantly superior to those of placebo, similar to those of tricyclic antidepressants (TCAs) [amitriptyline, clomipramine and doxepin] and possibly superior to those of trazodone. Short term clinical tolerability data suggest that mirtazapine produces fewer anticholinergic-, adrenergic- and serotonergic-related adverse events than TCAs. In rare cases, mirtazapine, in common with many antidepressants, wasassociated with potentially serious changes in haematological parameters (e.g. agranulocytosis and neutropenia). The drug appears to be safe in overdose and possesses a very low propensity for inducing seizures. Comparisons with other classes of antidepressants are needed to determine the relative position of mirtazapine in clinical practice. However, preliminary data indicate that mirtazapine, with its novel mechanism of

action, is a promising addition to currently available options for the treatment of depression.

ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:

1998:426105 HCAPLUS 129:225564

Characterization of enhances behavioral responses to L-DOPA following repeated administration in the 6-hydroxydopamine-lesioned rat model of Parkinson's disease

AUTHOR(S): CORPORATE SOURCE:

SOURCE:

Henry, Brian; Crossman, Alan R.; Brotchie, Jonathan M. Manchester Movement Disorder Laboratory, Division of Neuroscience, School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK Experimental Neurology (1998), 151(2), 334-342

CODEN: EXNEAC; ISSN: 0014-4886

PUBLISHER: Academic Press

DOCUMENT TYPE: LANGUAGE:

Journal English

English Long-term treatment of Parkinson's disease with dopamine-replacing agents such as L-3,4-dihydroxy-phenylalanine (L-DOPA) is compromised by many side-effects, most notably involuntary movements, L-DOPA-induced dyskinesia. Acute challenge with dopamine-replacing drugs elicits a rotational response in the 6-hydroxydopamine (6-OHDA)-lesioned rat model of Parkinson's disease. This rotation is contraversive to the lesion and is considered to represent an antiparkinsonian effect. More recently, it has become clear that the rotational response shows plasticity and that repeated L-DOPA or apomorphine therapy is accompanied by a marked enhancement in this response. In this study, the authors demonstrate that the enhanced behavioral response to repeated dopamine-replacement therapy seen in the 6-OHDA-lesioned rat has pharmacol. characteristics similar to L-DOPA-induced dyskinesia seen in MPTP-lesioned primates and man. the magnitude and rate of development of the enhanced response to L-DOPA treatment is related to both the no. of doses and the size of the dose of L-DOPA administered. In contrast, de novo administration of dopaminergic drugs that are assocd. with a lower incidence of dyskinesia, e.g., bromocriptine or lisuride, does not lead to an enhanced behavioral response following repeated treatment. However, following a single "priming" administration of apomorphine, the rotational response elicited by subsequent bromocriptine administrations is enhanced with repeated treatment. Once established, the enhanced behavioral response to repeated L-DOPA-administration (6.5 mg/kg, twice daily) can, like L-DOPA-induced dyskinesia in man and MPTP-treated monkeys, be selectively reduced by coadministration of L-DOPA with the alpha2-adrenergic receptor antagonist yohimbine (10 mg/kg, -95%), the 5-HT

a-adrenergic  $\mathbb{Z}$ -MDOT (2 mg/kg, -90%), or the receptor antagonist propranolol (10 mg/kg, -35%). While these rats do not exhibit symptoms of dyskinesia per se, this rodent model does exhibit behaviors, the underlying mechanism of which is likely to be similar to that underlying L-DOPA-induced dyskinesia and may prove useful in studying the mol. and cellular mechanisms of L-DOPA-induced dyskinesia in Parkinson's disease. (c) 1998 Academic Press.

1-11 (Pharmacology) CC

behavior sensitization DOPA parkinsonism dyskinesia; dopaminergic drug behavior sensitization parkinsonism dyskinesia

Antiparkinsonian agents

Dopamine agonists

(characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in relation to induction of dyskinesia)

Toxicity ΙT

(drug; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in relation to induction of dyskinesia)

Nervous system IT

(dyskinesia; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in relation to induction of dyskinesia)

IT Behavior

(rotational; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in relation to induction of dyskinesia)

Behavior TT

(sensitization; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in relation to induction of dyskinesia)

7101-51-1, L-DOPA methyl ester 58-00-4, Apomorphine IT25614-03-3, Bromocriptine

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of Parkinson's disease in

relation to induction of dyskinesia)

THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS 40 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT REFERENCE COUNT:

ACCESSION NUMBER: DOCUMENT NUMBER: TITLE:

CORPORATE SOURCE:

1991:74612 HCAPLUS 114:74612

A novel in vivo test for drugs affecting central serotonergic and adrenergic systems

Rawlow, Andrew; King, Roger G.

Dep. Pharmacol., Monash Univ., Clayton, 3168,

Australia

European Journal of Pharmacology (1990), 191(3),

263-72

CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE:

AUTHOR(S):

SOURCE:

Journal English

LANGUAGE: In urethane anesthetized rats, myoclonic twitches of the anterior digastricus muscle were evoked by L-5-hydroxytryptophan (L-5-HTP, 50-100 mg/kg i.v.), the serotonin (5-HT) receptor agonist, quipazine (1-8 mg/kg i.v.) and the 5-HT releaser, fenfluramine (4-8 mg/kg i.v.). The effect of L-5-HTP or quipazine on the frequency of twitches was inhibited by the 5-HT receptor antagonist cyproheptadine. Also L-DOPA (100 mg/kg i.p.) or the .alpha.1-adrenoceptor agonist, cirazoline (0.3-3 mg/kg i.v.) evoked twitches of the muscle which were inhibited by the .alpha.1-adrenoceptor antagonist, prazosin. In decerebrate, artificially respired rats, neither L-5-HTP nor L-DOPA evoked the twitches. The frequency of twitches evoked by fenfluramine but not by L-DOPA was increased by the .alpha.2-adrenoceptor agonist, clonidine (0.2 and 0.4 mg/kg i.v.); clonidine's effect was abolished by the .alpha.2 -adrenoceptor antagonist, yohimbine. The .beta.2-adrenoceptor agonist, salbutamol (0.01-1 mg/kg i.v.) had no effect on fenfluramine-induced twitches. It is concluded that (1) activation of 5-HT receptors or .alpha.1-adrenoceptors in the brain of urethane-anesthetized rats evokes twitches of the anterior digastricus muscle, and (2) this prepn. can be utilized as a test to study the action of compds. on central 5-HT and adrenergic systems.

CC 1-1 (Pharmacology)